

FISYDGSNKHYADSVKG (SEQ ID NO:33) and TGWLGPFDY (SEQ ID NO: 37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVSSSFLA (SEQ ID NO:25), GASSRAT (SEQ ID NO:30), and QQYGSSPWT (SEQ ID NO:35), respectively.

Please replace the paragraph beginning on page 7, line 13, with the following amended paragraph:

Other human sequence antibodies of the invention comprise heavy chain CDR1, CDR2, and CDR3 sequences, SYGMH (SEQ ID NO:28), VIWYDGSNKYYADSVKG (SEQ ID NO:34) and APNYIGAFDV (SEQ ID NO:38), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQGISSWLA (SEQ ID NO:26), AASSLQS (SEQ ID NO:31), and QQYNSYPPT (SEQ ID NO:36), respectively.

Please replace the paragraph beginning on page 8, line 3, with the following amended paragraph:

The invention provides a hybridoma cell line comprising a B cell obtained from a transgenic non-human animal having a genome comprising a human sequence heavy chain transgene and a human sequence light chain transgene, wherein the hybridoma produces a human sequence antibody that specifically binds to human CTLA-4. In a related embodiment, the hybridoma secretes a human sequence antibody that specifically binds human CTLA-4 or binding fragment thereof, wherein the antibody is selected from the group consisting of: a human sequence antibody comprising heavy chain heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH (SEQ ID NO:27), FISYDGNNKYYADSVKG (SEQ ID NO:32) and TGWLGPFDY (SEQ ID NO:37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVGSSYLA (SEQ ID NO:24), GAFSRAT (SEQ ID NO:29), and QQYGSSPWT (SEQ ID NO:35), respectively, and heavy chain and light chain variable region amino acid sequences as set forth in SEQ ID NO:17 and SEQ ID NO:7, respectively; a human sequence antibody comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH (SEQ ID NO:27), FISYDGSNKHYADSVKG

(SEQ ID NO:33) and TGWLGPFDDY (SEQ ID NO: 37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVSSSFLA (SEQ ID NO:25), GASSRAT (SEQ ID NO:30), and QQYGSSPWT (SEQ ID NO:35), respectively, and heavy chain and light chain variable region amino acid sequences as set forth in SEQ ID NO:19 and SEQ ID NO:9, respectively; or a human sequence antibody of claim 1, comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYGMH (SEQ ID NO:28), VIWYDGSNKYYADSVKG (SEQ ID NO:34) and APNYIGAFDV (SEQ ID NO:38), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQGISSWLA (SEQ ID NO:26), AASSLQS (SEQ ID NO:31), and QQYNSYPPT (SEQ ID NO:36), respectively, and heavy chain and light chain variable region amino acid sequences as set forth in SEQ ID NO:23 and SEQ ID NO:13, respectively.

Please replace Table 3, on page 72, lines 1-4, with the following amended table:

Chain	HuMAb	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
<b>Light Chain</b>	10D1	RASQSVGSSYLA	24	GAFSRAT	29	QQYGSSPWT	35
	4B6	RASQSVSSSFLA	25	GASSRAT	30	QQYGSSPWT	35
	1E2	RASQGISSWLA	26	AASSLQS	31	QQYNSYPPT	36
<b>Heavy Chain</b>	10D1	SYTMH	27	FISYDGNKYYADSVKG	32	TGWLGPFDY	37
	4B6	SYTMH	27	FISYDGSNKHYADSVKG	33	TGWLGPFDY	37
	1E2	SYGMH	28	VIWYDGSNKYYADSVKG	34	APNYIGAFDV	38

Please replace the paragraph beginning on page 76, line 16, with the following amended paragraph:

The kappa light chain plasmid, pCK7-96 (SEQ ID NO:39), includes the kappa constant region and polyadenylation site, such that kappa sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and BbsI, and cloned into pCK7-96 digested with HindIII and BbsI to reconstruct a complete light chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/NotI fragment

and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

Please replace the paragraph beginning on page 76, line 23, with the following amended paragraph:

The gamma1 heavy chain plasmid, pCG7-96 (SEQ ID NO:40), includes the human gamma1 constant region and polyadenylation site, such that gamma sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and AgeI, and cloned into pCG7-96 digested with HindIII and AgeI to reconstruct a complete gamma1 heavy chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/SalI fragment and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

Please replace the paragraph beginning on page 76, line 31, with the following amended paragraph:

The gamma4 heavy chain plasmid, pG4HE (SEQ ID NO:41), includes the human gamma4 constant region and polyadenylation site, such that gamma sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and AgeI, and cloned into pG4HE digested with HindIII and AgeI to reconstruct a complete gamma4 heavy chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/EcoRI fragment and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

Please insert the following paragraph immediately before the paragraph beginning at page 93, line 1 of the specification:

SEQ ID NO:1 pGP1k

AATTAGCGGC CGCTGTCGAC AAGCTTCGAA TTCAGTATCG ATGTGGGGTA	50
CCTACTGTCC CGGGATTGCG GATCCGCGAT GATATCGTTG ATCCTCGAGT	100
GCGGCCGCGAG TATGCAAAAA AAAGCCCGCT CATTAGGCGG GCTCTTGGCA	150
GAACATATCC ATCGCGTCCG CCATCTCCAG CAGCCGCACG CGGCGCATCT	200
CGGGCAGCGT TGGGTCCTGG CCACGGGTGC GCATGATCGT GCTCCTGTCTG	250

TTGAGGACCC GGCTAGGCTG GCGGGGTTGC CTTACTGGTT AGCAGAATGA 300  
ATCACCGATA CGCGAGCGAA CGTGAAGCGA CTGCTGCTGC AAAACGTCTG 350  
CGACCTGAGC AACAACATGA ATGGTCTTCG GTTTCCTGTG TTCGTAAAGT 400  
CTGGAACCGC GGAAGTCAGC GCCCTGCACC ATTATGTTCC GGATCTGCAT 450  
CGCAGGATGC TGCTGGCTAC CCTGTGGAAC ACCTACATCT GTATTAACGA 500  
AGCGCTGGCA TTGACCCTGA GTGATTTTTC TCTGGTCCCG CCGCATCCAT 550  
ACCGCCAGTT GTTTACCCTC ACAACGTTCC AGTAACCGGG CATGTTTCATC 600  
ATCAGTAACC CGTATCGTGA GCATCCTCTC TCGTTTCATC GGTATCATT 650  
CCCCCATGAA CAGAAATTCC CCCTTACACG GAGGCATCAA GTGACCAAAC 700  
AGGAAAAAAC CGCCCTTAAC ATGGCCCGCT TTATCAGAAG CCAGACATTA 750  
ACGCTTCTGG AGAAACTCAA CGAGCTGGAC GCGGATGAAC AGGCAGACAT 800  
CTGTGAATCG CTTACGACC ACGCTGATGA GCTTTACCGC AGCTGCCTCG 850  
CGCGTTTCGG TGATGACGGT GAAAACCTCT GACACATGCA GCTCCCGGAG 900  
ACGGTCACAG CTTGTCTGTA AGCGGATGCC GGGAGCAGAC AAGCCCGTCA 950  
GGGCGCGTCA GCGGGTGTG GCGGGTGTG GGGCGCAGCC ATGACCCAGT 1000  
CACGTAGCGA TAGCGGAGTG TATACTGGCT TAACATGCG GCATCAGAGT 1050  
AGATTGTACT GAGAGTGCAC CATATCGGT GTGAAATACC GCACAGATGC 1100  
GTAAGGAGAA AATACCGCAT CAGGCGCTCT TCCGCTTCCT CGCTCACTGA 1150  
CTCGCTGCGC TCGGTCTGTT GGCTGCGGCG AGCGGTATCA GCTCACTCAA 1200  
AGGCGGTAAT ACGGTTATCC ACAGAATCAG GGGATAACGC AGGAAAGAAC 1250  
ATGTGAGCAA AAGGCCAGCA AAAGGCCAGG AACCGTAAAA AGGCCGCGTT 1300  
GCTGGCGTTT TTCCATAGGC TCCGCCCCCC TGACGAGCAT CACAAAAATC 1350  
GACGCTCAAG TCAGAGGTGG CGAAACCCGA CAGGACTATA AAGATACCAG 1400  
GCGTTTCCCC CTGGAAGCTC CCTCGTGCGC TCTCCTGTTT CGACCCTGCC 1450  
GCTTACCGGA TACCTGTCCG CCTTCTCCC TTCGGGAAGC GTGGCGCTTT 1500  
CTCATAGCTC ACGCTGTAGG TATCTCAGT CGGTGTAGGT CGTTCGCTCC 1550  
AAGCTGGGCT GTGTGCACGA ACCCCCCGTT CAGCCCGACC GCTGCGCCTT 1600  
ATCCGGTAAC TATCGTCTTG AGTCCAACCC GGTAAGACAC GACTTATCGC 1650  
CACTGGCAGC AGCCAGGCGC GCCTTGGCCT AAGAGGCCAC TGGTAACAGG 1700  
ATTAGCAGAG CGAGGTATGT AGGCGGTGCT ACAGAGTTCT TGAAGTGGTG 1750  
GCCTAACTAC GGCTACACTA GAAGGACAGT ATTTGGTATC TGCGCTCTGC 1800  
TGAAGCCAGT TACCTTCGGA AAAAGAGTTG GTAGCTCTTG ATCCGGCAAA 1850  
CAAACCACCG CTGGTAGCGG TGGTTTTTTT GTTTGCAAGC AGCAGATTAC 1900  
GCGCAGAAAA AAAGGATCTC AAGAAGATCC TTTGATCTTT TCTACGGGGT 1950  
CTGACGCTCA GTGGAACGAA AACTCACGTT AAGGGATTTT GGTCATGAGA 2000  
TTATCAAAAA GGATCTTCAC CTAGATCCTT TTAATTTAAA AATGAAGTTT 2050  
TAAATCAATC TAAAGTATAT ATGAGTAAAC TTGGTCTGAC AGTTACCAAT 2100  
GCTTAATCAG TGAGGCACCT ATCTCAGCGA TCTGTCTATT TCGTTCATCC 2150  
ATAGTTGCCT GACTCCCCGT CGTGTAGATA ACTACGATAC GGGAGGGCTT 2200  
ACCATCTGGC CCCAGTGCTG CAATGATACC GCGAGACCCA CGCTCACCGG 2250  
CTCCAGATTT ATCAGCAATA AACCAGCCAG CCGGAAGGGC CGAGCGCAGA 2300  
AGTGGTCCTG CAACTTTATC CGCCTCCATC CAGTCTATTA ATTGTTGCCG 2350  
GGAAGCTAGA GTAAGTAGTT CGCCAGTTAA TAGTTTGCGC AACGTTGTTG 2400  
CCATTGCTGC AGGCATCGTG GTGTCACGCT CGTCGTTTGG TATGGCTTCA 2450  
TTCAGCTCCG GTTCCCAACG ATCAAGGCGA GTTACATGAT CCCCCATGTT 2500  
GTGCAAAAAA GCGGTTAGCT CTTTCGGTCC TCCGATCGTT GTCAGAAGTA 2550  
AGTTGGCCGC AGTGTTATCA CTCATGGTTA TGGCAGCACT GCATAATTCT 2600  
CTTACTGTCA TGCCATCCGT AAGATGCTTT TCTGTGACTG GTGAGTACTC 2650  
AACCAAGTCA TTCTGAGAAT AGTGTATGCG GCGACCGAGT TGCTCTTGCC 2700  
CGGCGTCAAC ACGGGATAAT ACCGCGCCAC ATAGCAGAAC TTAAAAAGTG 2750  
CTCATATTAG GAAAACGTTT TTCGGGGCGA AAACCTCTCA GGATCTTACC 2800  
GCTGTTGAGA TCCAGTTTCA GTAAACCCAC TCGTGCAACC AACTGATCTT 2850  
CAGCATCTTT TACTTTCACC AGCGTTTCTG GGTGAGCAAA AACAGGAAGG 2900  
CAAAATGCCG CAAAAAAGGG AATAAGGGCG ACACGGAAAT GTTGAATACT 2950  
CATACTCTTC CTTTTTCAAT ATTATTGAAG CATTTATCAG GGTTATTGTC 3000  
TCATGAGCGG ATACATATTT GAATGTATTT AGAAAAATAA ACAAATAGGG 3050

GTTCGCGCA CATTTCCTCCG AAAAGTGCCA CCTGACGTCT AAGAAACCAT 3100  
TATTATCATG ACATTAACCT ATAAAAATAG GCGTATCACG AGGCCCTTTC 3150  
GTCTTCAAG 3159

Please replace the paragraph beginning on page 93, line 1, with the following amended paragraph:

**pCK7-96 (Nucleotide residues 3376 to 3881)(SEQ ID NO:39)**

AGGAGAATGAATAAATAAAGTGAATCTTTGCACCTGTGGTTTCTCTCTTTCTCCTCAATTTAATAATTATT  
ATCTGTTGTTTACCAACTACTCAATTTCTCTTATAAGGGACTAAATATGTAGTCATCCTAAGGCGCATA  
ACCATTTATAAAAAATCATCCTTCATTCTATTTTACCCTATCATCCTCTGCAAGACAGTCCTCCCTCAAA  
CCCACAAGCCTTCTGTCTCACAGTCCCCTGGGCCATGGATCCTCACATCCCAATCCGCGGCCGCAATT  
CGTAATCATGGTCATAGCTGTTTCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAG  
CCGGAAGCATAAAGTGTAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCT  
CACTGCCCCTTTCCAGTCGGGAAACCTGTCTGCGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGA  
GAGGCGGTTTGCGTATTGGGCGC

Please replace the paragraph beginning on page 93, line 8, with the following amended paragraph:

**pCG7-96 (SEQ ID NO:40)**

Please replace the paragraph beginning on page 94, line 12, with the following amended paragraph:

**pG4HE (SEQ ID NO:41)**

Please replace the paragraph beginning on page 95, line 17, with the following amended paragraph:

**10D1 VH(SEQ ID NO:16)**

Please replace the paragraph beginning on page 95, line 27, with the following amended paragraph:

**10D1 VK(SEQ ID NO:6)**

Please replace the paragraph beginning on page 95, line 37, with the following amended paragraph:

**4B6 VH(SEQ ID NO:18)**